

Remarks

A. Status of Claims.

Claims 1-11 are pending. Herein, claims 1-10 have been amended. These amendments simply reflect Applicant's desire to use preferred terminology, and each amendment is fully supported by the specification.

B. Introduction.

Paper No. 7 set forth a nine-way restriction requirement. Applicant respectfully traverses the restriction with regard to groups I-VIII, although he provisionally elects to have the claims of group I, namely claims 1-3 and 5, examined in this application. That said, Applicant respectfully requests reconsideration and withdrawal of the restriction requirement as it relates to the claims of groups II-VIII for the reasons stated below. Applicant also reserves the right to cancel non-elected claims and/or add new claims up through the time a response to a notice of allowable subject matter is submitted.

C. Response.

The instant application contains two independent claims, claims 1 and 6. The other claims each depend, directly or indirectly, from either of these two claims. Claims 1-10 are each directed to compositions of matter that comprise artificial antigen presenting cells ("aAPCs") having at least certain specified elements. Specifically, the aAPCs of claim 1 comprise a liposome formed by a lipid bilayer. Disposed in or otherwise associated with the lipid bilayer are at least several types of components, including GM-1 components, cholera toxin β subunit components, MHC components loaded with antigen, and accessory molecule components. The aAPCs of claim 6 also contain these components, and additionally tetraavidin components that bind to GM-1 components and accessory molecule components. Thus, it is clear that independent claims 1 and 6 differ only in that the aAPCs of claim 6 further comprises tetraavidin. As such, the aAPCs of claim 6 represent a sub-genus of the genus of aAPCs defined by claim 1.¹

Despite the clear close relationship of the claims, as demonstrated by such factors claim dependence, genus/sub-genus status, and identity as to search classification (even at the

¹ Discussion of claim 11, drawn to methods of modulating antigen-specific T cells and dependent on either of claims 1 and 6, is deferred because it concerns presently non-elected subject matter.

level of sub-class), the Examiner posits that the subject matter bounded by claims 1-10 actually represents eight independent and distinct inventions, each being a "different product". Indeed, the subject matter defined by claims 4 and 9 alone is said to concern six independent and distinct inventions, or "products", represented by groups II-IV and VI-VIII in Paper No. 7. Restriction is purportedly required because,

"The products comprise different components with different immunological properties. For example, the addition of co-stimulatory components would significantly alter the composition's immunostimulatory capacity whereas the addition of adhesion components might alter the composition's immunolocalizing properties. Therefore the methods² are patentably distinct." Paper No. 7, p. 3.

Applicants respectfully submit that the instant restriction is improper. As discussed above, independent claim 1 contains several specified components, namely a lipid bilayer, GM-1 components, cholera toxin β subunit components, MHC components loaded with antigen, and accessory molecule components. Because this claim is "open", i.e., it uses the transition "comprising", other components can also be included. Claim 2 concerns such aAPCs wherein the GM-1 components form "rafts" in the lipid bilayer, and claim 3 (dependent from claim 2) specifies that the rafts be present in the lipid bilayer in high density. Claim 4, which depends from claim 3, specifies that the aAPC further comprises at least one "immunologically active molecule", *e.g.*, a co-stimulatory molecule, an adhesion molecule, a cell adhesion molecule, or a combination of any of the foregoing. Claim 5, which also depends from claim 3, is directed to aAPCs that further comprise at least one "irrelevant molecule", *e.g.*, a label or a molecule for binding the aAPC to a solid support. Applicant respectfully submits that these aAPCs do not comprise "different components". To the contrary, the aAPCs of each of claims 1-5 comprise each and every element recited in claim 1. The fact that the aAPCs of claims 4 and 5 each further comprise an additional element, "immunologically active molecules" in the case of claim 4 and an one or more "irrelevant molecules" in the case of claim 5, does not make them a "different product" as compared to the aAPCs of claim 1. Claims 4 and 5 instead represent further definition of an aAPC according to claim 3, and hence, indirectly, the aAPCs of claim 1. Put another way, the aAPCs of claims 4 and 5 represent independent sub-genera of the genus of

² Applicant notes none of claims of groups I-VIII are drawn to "methods", but instead relate to compositions of matter. Applicant presumes that use of the term "method" in this instance was an oversight.

aAPCs defined by claim 1. Such further definition is completely appropriate in the context of claiming one's invention. If such practice was not allowed, each patent would necessarily contain but one claim. The patent laws set forth in Title 35 of the United States Code are expressly contrary to a "one patent, one claim" paradigm, providing that, "The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. §112, 2nd ¶.

In addition to express statutory permission to use multiple claims, even multiple independent claims, to define an invention, the Patent Office provides for this as well. No clearer evidence of this is the fee schedule for claims filed in connection with a patent application. There, additional fees are charged for each claim in excess of 20, as are fees for more than three independent claims.

Notwithstanding the foregoing, Applicant appreciates and acknowledges that restriction practice serves the purpose of limiting a patent application to claims directed to a single invention. See 35 U.S.C. §121, 37 CFR 1.141, MPEP §800. Given the obvious risks associated with issuing requirements for restriction, however, clear rules have long existed to prevent abuse. Specifically, Patent Office practice mandates that restriction is proper only when each of two criteria are met: that the inventions are independent or distinct as claimed; and that a serious burden rests on the examiner to examine each invention. MPEP §803.

In this case, there is no need to address the criterion about "independence" or "distinctness" because no *prima facie* showing of a serious burden has been made. The MPEP states that, "a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation of separate classification, or separate status in the art, or a different field of search". MPEP § 803, guidelines. Paper No. 7 makes clear that the subject matter of all of the pending claims has the same classification and sub-classification, namely Class 424, subclass 93.1. Such identity in terms of classification and sub-classification also eliminates the need for different fields of search. Left with only one option to establish a *prima facie* showing, the Examiner simply alleges that the subject matter of claims 1-10 has "acquired a separate status in the art because of their recognized divergent subject matter". Paper No. 7, ¶4. Applicant respectfully disagrees, contending that such reasoning is in error because it focuses not on the invention as claimed, but on differences among molecules that comprise just a single element of the claims, specifically, the "immunologically active molecule" of claims 4 and 9 or the

tetraavidin moiety of claim 6. When viewed in their totality, however, it is manifestly clear that the claimed artificial antigen presenting cells in groups I-VIII could not have acquired a separate art-recognized status since each and every claim relates to the same pioneering invention, namely artificial antigen presenting cells each of which must minimally possess the components recited in claim 1. Even if each of the "immunologically active molecule" types of claims 4 and 9 are "divergent", and even if independent claim 6 contains one or more elements in addition to those recited in claim 1, because the artificial antigen presenting cells of each of the claims of groups I-VIII themselves have not acquired any status (due to their pioneering nature), let alone a separate status, in the art, no *prima facie* showing of a serious burden has been made. For this reason, there is no basis for restricting any of claims 1-10 into two or more groups. The restriction requirement as it relates to claims 1-10 should thus be withdrawn, and each of these claims should be included in group 1, along with claims 1-3 and 5.

Conclusion

Herein, Applicant has amended certain of the pending claims. He also provisionally elects to have claims 1-3 and 5 substantively examined in this application, while at the same time demonstrating why restriction as to claims 4 and 6-10 is improper. As such, Applicant respectfully requests that the restriction advanced in Paper No. 7 be withdrawn, at least with respect to claims 1-10, and that at least these claims be examined in this application.

Applicant also wishes to note that this application is of critical importance to the assignee, Androclus Therapeutics, SpA. Accordingly, Applicant respectfully requests that if any matter arises during prosecution that can be dealt with appropriately without the need for a formal action and response thereto, the Examiner is encouraged to call the undersigned at his earliest convenience so that the same may be addressed in a timely manner.

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Appendix A

Version with marking to show changes made.

Below please find a copy of the amended claims and application title marked to show all changes in the version of the claims and specification now pending. In the marked copy, added material is underlined and deleted material is interlined.

A. Claims

See attached pages A-1 through A-3.

B. Application Title

See attached page A-4.



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1. (amended) An artificial antigen presenting cell, comprising:
 - a) ~~a liposome components, said components forming~~comprising a lipid bilayers of a liposome;
 - b) ~~GM-1 components, said GM-1 comprising at least one GM-1 molecule disposed in the lipid bilayer, said GM-1 contacting said liposome components;~~
 - c) ~~cholera toxin β subunit components, said β subunit components comprising at least a portion of said a cholera toxin β subunit capable of binding to~~associated with a GM-1 molecule;
 - d) ~~an immunologically active MHC component loaded with an antigens, wherein the said antigen-loaded MHC components comprising immunologically active molecules and contacting at is associated with least said the cholera toxin β subunit; and~~
 - e) ~~antigen components, said antigen components contacting at least said MHC components; and~~
 - f) ~~an accessory molecule components, said accessory molecule components providing for a that can stabilizeing property to an interaction between a T cell receptor and said the antigen-loaded MHC and said antigen components.~~
2. (amended) An artificial antigen presenting cell according to claim 1 ~~wherein said~~having a plurality of GM-1 ~~components~~ molecules, wherein a portion of the GM-1 molecules form rafts ~~comprising multiples of said GM-1 molecules in said the lipid bilayers of the liposome.~~
3. (amended) An artificial antigen presenting cell according to claim 2 wherein ~~said the~~ rafts are present in ~~said the~~ lipid bilayer at high density.
4. (amended) An artificial antigen presenting cell according to claim 3 further comprising one or more immunologically active molecules each selected from the group consisting of co-stimulatory molecules, adhesion molecules, ~~and~~ cell modulation molecules, and combinations of one or more of a co-stimulatory molecule, an adhesion molecule, and a cell modulation molecule.

5. (amended) An artificial antigen presenting cell according to claim 3 further comprising one or more irrelevant molecules each selected from the group consisting of molecules for binding said artificial antigen presenting cell to a solid support, and a label, and a combination of support-binding molecules and labels.

6. (amended) An artificial antigen presenting cell, comprising:
 - a) a liposome comprising a components, said components forming lipid bilayers of a liposome;
 - b) GM-1 components, said GM-1 comprising at least one GM-1 molecule disposed in the lipid bilayer, said GM-1 contacting said liposome components;
 - c) cholera toxin β subunit components, said β subunit components comprising at least a portion of a cholera toxin β said subunit capable of binding to associated with a GM-1 molecule;
 - d) at least one tetraavidin molecule associated with the lipid bilayer components, said tetraavidin capable of binding to said cholera toxin, said tetraavidin further capable of binding between 1 and 3 immunologically active molecules;
 - e) an immunologically active MHC component loaded with an antigens, wherein the said MHC components is associated with the comprising immunologically active molecules and contacting at least said cholera toxin β subunit; and
 - f) antigen components, said antigen components contacting at least said MHC components; and
 - g) f) an accessory molecule components, said accessory molecule components providing for a that can stabilize ing property to an interaction between a T cell receptor and said the antigen-loaded MHC and said antigen components, wherein said the accessory molecule is associated with a tetraavidin molecule s comprising said immunologically active molecules of (d).

7. (amended) An artificial antigen presenting cell according to claim 6 wherein said having a plurality of GM-1 components molecules, wherein a portion of the GM-1

molecules form rafts comprising multiples of said GM-1 molecules in said the lipid bilayers of the liposome.

8. (amended) An artificial antigen presenting cell according to claim 7 wherein said the rafts are present in said the lipid bilayer at high density.

9. (amended) An artificial antigen presenting cell according to claim 8 further comprising one or more immunologically active molecules each selected from the group consisting of co-stimulatory molecules, adhesion molecules, and cell modulation molecules, and combinations of one or more of a co-stimulatory molecule, an adhesion molecule, and a cell modulation molecule.

10. (amended) An artificial antigen presenting cell according to claim 8 further comprising one or more irrelevant molecules each selected from the group consisting of molecules for binding said artificial antigen presenting cell to a solid support, and a label, and a combination of support-binding molecules and labels.

Methods for Isolation, Quantification, Characterization and Modulation of Antigen-Specific T Cells Artificial Antigen Presenting Cells